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Application Serial No. 10/599,461 Atty Docket No. INFA-00101-NUS

01/07/2010

## Amendments to the Claims:

- 1. (Currently amended) A process for the preparation of the  $\alpha$ -crystal form of the methanesulfonic acid addition salt of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[4-pyridin-3-yl)pyrimidin-2-ylamino]phenyl]benzamide comprising:
  - a) carrying out an acid addition reaction using not more than 0.99 equivalents of methanesulfonic acid per 1 equivalent of 4-(4methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide, in a solvent selected from the group consisting of C<sub>2</sub>-C<sub>6</sub> aliphatic alcohols and the mixtures thereof, optionally with the addition of a C<sub>1</sub>-C<sub>4</sub> aliphatic alcohol;
  - b) optionally adding a solvent selected from the group consisting of esters formed from a C<sub>1</sub>-C<sub>4</sub> aliphatic alcohol and formic acid, acetic acid, or propionic acid;
  - c) optionally inoculating the reaction mixture with the  $\alpha$ -crystal form;
  - d) stirring the reaction mixture for the time necessary for crystallization of the  $\alpha$ -crystal form; and
  - e) isolating the  $\alpha$ -crystal form from the reaction mixture, wherein said α-crystal form of the methanesulfonic acid addition salt of 4-(4methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2ylamino)phenyl]benzamide isolated from the reaction mixture shows an Xray powder diffraction pattern that is characterized by having peaks at  $2\theta$ angles of approximately: 4.9; 18.6; 19.1; 23.2 and 28.6°.
- 2. (Original) The process according to claim 1 in which the acid addition reaction is carried out using from 0.95 to 0.99 equivalents of methanesulfonic

- acid per 1 equivalent of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl] benzamide.
- 3. (Previously presented) The process according to claim 1, in which the acid addition reaction is carried out in an alcohol selected from the group consisting of *n*-propyl alcohol, isopropyl alcohol, *n*-butyl alcohol, *tert*-butyl alcohol, and the mixtures thereof with ethyl alcohol.
- 4. (Previously presented) The process according to claim 1, in which the acid addition reaction is carried out in a mixture of solvents containing from 0 to 50% of ethyl alcohol and from 50 to 100% of n-propyl alcohol (v/v).
- 5. (Previously presented) The process according to claim 1 in which the acid addition reaction is carried out in the mixture of solvents containing from 0 to 50% of ethyl alcohol and from 50 to 100% of isopropyl alcohol (v/v).
- 6. (Previously presented) The process according to claims 1 in which the acid addition reaction is carried out in a mixture of solvents containing from 0 to 50% of ethyl alcohol and from 50 to 100% of n-butyl alcohol (v/v).
- 7. (Previously presented) The process according to claims 1 in which the acid addition reaction is carried out in a mixture of solvents containing from 0 to 50% of ethyl alcohol and from 50 to 100% of *tert*-butyl alcohol (v/v).
- 8. (Currently amended) A process for the preparation of the α-crystal form of the methanesulfonic acid addition salt of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[4-pyridin-3-yl)pyrimidin-2-ylamino]phenyl]benzamide comprising:
  - a) carrying out an acid addition reaction using 1 equivalent of methanesulfonic acid per 1 equivalent of 4-(4-methylpiperazin-1-

- ylmethyl)-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide in the ethyl alcohol, optionally with the addition of a C<sub>1</sub>-C<sub>4</sub> aliphatic alcohol;
- b) adding a solvent selected from the group consisting of esters formed from a C<sub>1</sub>-C<sub>4</sub> aliphatic alcohol and formic acid, acetic acid, or propionic acid;
- c) inoculating the reaction mixture with the  $\alpha$ -crystal form;
- d) stirring the reaction mixture for the time necessary for crystallization of the  $\alpha$ -crystal form; and
- e) isolating the α-crystal form from the reaction mixture, wherein said α-crystal form of the methanesulfonic acid addition salt of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide isolated from the reaction mixture shows an X-ray powder diffraction pattern that is characterized by having peaks at 2θ angles of approximately: 4.9; 18.6; 19.1; 23.2 and 28.6°.
- 9. (Previously presented) The process according to claim 8 wherein said  $C_1$ - $C_4$  aliphatic alcohol is methyl alcohol or isopropyl alcohol, and the proportion of said  $C_1$ - $C_4$  aliphatic alcohol to other solvents present in the reaction mixture do not exceed 55% (v/v).
- 10. (Previously presented) The process according to claim 1 in which the acid addition reaction is carried out with stirring while maintaining the internal temperature of the reaction mixture within the range from room temperature to boiling temperature.

## 11-12. (Canceled)

13. (Currently amended) The process according to claim 1 in which said α-crystal form of the methanesulfonic acid addition salt of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide isolated from the reaction mixture shows an X-ray powder diffraction pattern that is characterized by having peaks of relative intensity over 20% at 2θ angles of approximately: 4.9, 10.5; 14.9; 16.5; 17.7; 18.1; 18.6; 19.1; 21.3; 21.6; 22.7; 23.2; 23.8; 24.9; 27.4; 28.0 and 28.6°, the relative intensity being determined with respect to the most intense peak by peak height, the peak height expressing a number of counts per second.

## 14-23. (Canceled).

- 24. (Previously presented) The process according to claim 2, in which the acid addition reaction is carried out in an alcohol selected from the group comprising *n*-propyl alcohol, isopropyl alcohol, *n*-butyl alcohol, *tert*-butyl alcohol and the mixtures thereof with ethyl alcohol.
- 25. (Previously presented) The process according to claim 2 in which the addition reaction is carried out in the mixture containing from 0 to 50% of ethyl alcohol and from 50 to 100% of n-propyl alcohol (v/v).

#### 26-27. (Canceled)

28. (Currently amended) The process according to claims 2 in which said α-crystal form of the methanesulfonic acid addition salt of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide isolated from the reaction mixture shows an X-ray powder diffraction pattern that is characterized by having peaks at 2θ

angles of approximately: <u>4.9,</u> 10.5; 14.9; 16.5; 17.7; 18.1; 18.6; 19.1; 21.3; 21.6; 22.7; 23.2; 23.8; 24.9; 27.4; 28.0 and 28.6°.

29. (Previously presented) The process according to claim 8 in which the acid addition reaction is carried out with stirring while maintaining the internal temperature of the reaction mixture within the range from room temperature to boiling temperature.

# 30-31. (Canceled)

32. (Currently amended) The process according to claim 8 in which said α-crystal form of the methanesulfonic acid addition salt of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide isolated from the reaction mixture shows an X-ray powder diffraction pattern that is characterized by having peaks of relative intensity over 20% at 2θ angles of approximately: 4.9, 10.5; 14.9; 16.5; 17.7; 18.1; 18.6; 19.1; 21.3; 21.6; 22.7; 23.2; 23.8; 24.9; 27.4; 28.0 and 28.6°, the relative intensity being determined with respect to the most intense peak by peak height, the peak height expressing a number of counts per second.

## 33-36. (Canceled)

37. (Previously presented) The process of claim 8 wherein said α-crystal form of the methanesulfonic acid addition salt of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide isolated from the reaction mixture contains not more than 2% w/w of the β-crystal form of the methanesulfonic acid addition salt of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide.

38. (Previously presented) The process of claim 37 wherein said α-crystal form of the methanesulfonic acid addition salt of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide isolated from the reaction mixture contains not more than 1% w/w of the β-crystal form of the methanesulfonic acid addition salt of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-[(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide.